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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/018,672	04/18/2002	Joelle Thonnard	GSKB-120US	1681

26130 7590 01/30/2009

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EXAMINER	
BASKAR, PADMAVATHI	
ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
01/30/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/018,672	THONNARD, JOELLE	
	Examiner	Art Unit	
	Padma V. Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *55,57-59,61-63,68 and 73-84* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *55,57,59,62,63,68,73,74,77 and 78* is/are allowed.

6)☒ Claim(s) *58, 61, 75-76, 79-84* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/12/08* .
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants submission filed on 11/12/08 has been entered. MPEP 7.42.04.

Amendment

2. The amendment filed on 11/12/08 is acknowledged and entered.

Status of claims

3. Claims 1-54, 56 , 60, 64-67 and 69-72 are canceled
Claims 55 , 58, and 61 have been amended.
New claims 75- 84 have been added.
Claims 55, 57-59, 61-63, 68, 73-84 are pending and are under examination.

Information Disclosure Statement

4. The Information Disclosure Statement filed on 11/12/08 has been reviewed . It is noted page 3 contains two internet addresses , however, as it is not known what are these documents and the publication and page numbers, they are not considered and are lined through. All other references have been considered and a signed copy of the same is attached to this action.

Claim Rejections - 35 USC 112, first paragraph

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 58, 61, 75-76 and 79-84 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The Written Description Guidelines for examination of patent applications indicates, “the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical characteristics and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or

by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (see MPEP 2163).

Claims are drawn to an isolated recombinant polypeptide comprising an immunogenic fragment of at least 40 contiguous amino acids of SEQ ID NO: 2, wherein the immunogenic fragment, when administered either alone or coupled to a co-protein carrier is capable of inducing an antibody that specifically binds to said fragment within SEQ ID NO: 2, an isolated fusion protein and an immunogenic composition comprising said polypeptide. Thus, the scope of the claims includes a genus of "immunogenic fragments" and the genus is highly variant, inclusive to numerous fragments because a significant number of structural differences between genus members is permitted. The specification describes only a single isolated polypeptide comprising the (276 amino acids) amino acid sequence SEQ ID NO: 2 from *M.catarrhalis*. The specification does not place any structure, chemical or functional limitations on the fragments. The recitation of "immunogenic fragment of at least 40 contiguous amino acids of SEQ ID NO: 2," does not convey a common structure or function and is not so defined in the specification. For example, Roitt et al, 1998, Immunology, 4th ed, Mosby, London teach that although it is possible to produce antibodies to almost any part of an antigen, this does not normally happen in an immune response. It is usually found that only a certain areas of the antigen are particularly antigenic, and that a majority of antibodies bind to these regions. These regions are often at exposed areas on the outside of the antigen, particularly where there are loops of polypeptide that lack a rigid tertiary structure (p.7.7-7.8). This is exemplified by the teaching of Holmes (Exp. Opin.Invest. Drugs, 2001, 10(3):511-519) who teaches that rabbits were immunized with synthetic peptides which in each case generated high anti-peptide specific immunoreactivities, however, none of the antibodies exhibited binding to the full length antigen. "A patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when … the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed." *In re Curtis*, 354 F.3d 1347, 1358, 69 USPQ2d 1274, 1282 (Fed. Cir. 2004). For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. See, e.g., *Eli Lilly*.

Further, it is not sufficient to define it solely by its principal biological property, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property. Per the *Enzo* court's example, (*Enzo Biochem, Inc. v. Gen-Probe Inc.*, 63 USPQ2d 1609 (CA FC 2002) at 1616) of a description of an anti-inflammatory steroid, i.e., a steroid (a generic structural term) couched "in terms of its function of lessening inflammation of tissues" which, the court stated, "fails to distinguish any steroid from others having the same activity or function" and the expression "an antibiotic penicillin" fails to distinguish a particular penicillin molecule from others possessing the same activity and which therefore, fails to satisfy the written description requirement. Applicant has not disclosed any relevant, identifying characteristics, such as structure or other physical

and/or chemical properties, sufficient to show possession of the claimed genus. Mere idea or function is insufficient for written description; isolation and characterization at a minimum are required. A description of what a material does, rather than what it is, usually does not suffice. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

Structural features that could distinguish an "an isolated recombinant polypeptide comprising an immunogenic fragment of at least 40 contiguous amino acids of SEQ ID NO: 2" in the genus from others in the protein class are missing from the disclosure and the claims. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description, because specific, not general guidance is needed. Since the disclosure does not describe the common attributes or structural characteristics that identify members of the genus, and because the genus is highly variant, the function of binding alone is insufficient to describe the genus of "an isolated recombinant polypeptide comprising an immunogenic fragment of at least 40contiguous amino acids of SEQ ID NO: 2" of that function equivalently. One of skill in the art would reasonable conclude that the disclosure of a single "an isolated recombinant polypeptide comprising the amino acid sequence of SEQ ID NO: 2 does not provide a representative number of species of fragments of SEQ.ID.NO:2 that describe the claimed genus and as a consequence antibodies that bind such. The recitation of "an isolated recombinant polypeptide comprising an immunogenic fragment of at least 40 contiguous amino acids of SEQ ID NO: 2" does not convey a common structure or a common function. As such, generic polypeptide sequences that are unrelated via structure and function are highly variant and not conveyed by way of written description by the specification at the time of filing. As such the specification lacks written description for the highly variant genus of single function polypeptide and one skilled in the art would not recognize that applicants had possession of the genus of claimed "an isolated recombinant polypeptide comprising an immunogenic fragment of at least 40 contiguous amino acids of SEQ ID NO: 2", and a method of inducing in a mammal an antibody using said fragments as instantly claimed. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

7. Claims 58, 61, 75-76, 79-84 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inducing an antibody response in a mammal comprising administering to the mammal an isolated polypeptide comprising the amino acid sequence SEQ ID NO: 2 or a fusion protein or an immunogenic composition comprising said isolated polypeptide does not reasonably provide enablement for an isolated recombinant polypeptide comprising an immunogenic fragment of at least 40 contiguous amino acids of SEQ ID NO: 2, wherein the immunogenic fragment, when administered either alone or coupled to a co-protein carrier is capable of inducing an antibody that specifically binds to said fragment within SEQ ID NO: 2. The specification does not enable

any person skilled in the art to which it pertains, or with which it is most nearly connected to make and use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir.1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the breadth of the claims, (2) the nature of the invention, (3) the state of the prior art, (4) the predictability or unpredictability of the art, (5) the relative skill of those in the art, (6) the amount or direction or guidance presented, (7) the presence or absence of working examples, and (8) the quantity of experimentation necessary. Although the quantity of experimentation alone is not dispositive in a determination of whether the required experimentation is undue, this factor does play a central role. For example, a very limited quantity of experimentation may be undue in a fledgling art that is unpredictable where no guidance or working examples are provided in the specification and prior art, whereas the same amount of experimentation may not be undue when viewed in light of some guidance or a working example or the experimentation required is in a predictable established art. Conversely, a large quantity of experimentation would require a correspondingly greater quantum of guidance, predictability and skill in the art to overcome classification as undue experimentation. In Wands, the determination that undue experimentation was not required to make the claimed invention was based primarily on the nature of the art, and the probability that the required experimentation would result in successfully obtaining the claimed invention. (Wands, 8 USPQ2d 1406). Thus, a combination of factors which, when viewed together, would provide an artisan of ordinary skill in the art with an expectation of successfully obtaining the claimed invention with additional experimentation would preclude the classification of that experimentation as undue. A combination of Wands factors, which provide a very low likelihood of successfully obtaining the claimed invention with additional experimentation, however, would render the additional experimentation undue.

1-2 .Breadth of the claims and the nature of the invention.

In regards to the method of the claimed invention and the breadth of the claims the broadest interpretation that applies is fragments of fragment of 40 contiguous amino acids of SEQ ID NO: 2. The

nature of the invention is an isolated polypeptide comprising the amino acid sequence SEQ.ID.NO: 2 (276 amino acids) isolated from *M.catarrhalis* strain ATCC 43617 .

3-4. The state of prior art and the level of predictability in the art.

As drawn to epitopes**,** The state of the art of epitope identification for the induction of an immune response with linear peptides is as follows: Roitt et al, 1998, Immunology, 4th ed, Mosby, London teach that although it is possible to produce antibodies to almost any part of an antigen, this does not normally happen in an immune response. It is usually found that only a certain areas of the antigen are particularly antigenic, and that a majority of antibodies bind to these regions. These regions are often at exposed areas on the outside of the antigen, particularly where there are loops of polypeptide that lack a rigid tertiary structure (p.7.7-7.8). This is exemplified by the teaching of Holmes (Exp. Opin.Invest. Drugs, 2001, 10(3):511-519) who teaches that rabbits were immunized with synthetic peptides which in each case generated high anti-peptide specific immunoreactivities, however, none of the antibodies exhibited binding to the full length antigen. The author concludes that 'Presumably, expression of these epitopes in the context of the protein was important and affected the antibody binding ability (p. 513, col 1). Furthermore, this does not take into account the 3 dimensional folding of the native molecule, nor its glycosylation or other post-translational modifications and other characteristics which are of significant importance in an antibody response. Further, there is no teaching in the specification of which part of the protein should be used to produce antibodies which will bind specifically to an epitope within SEQ ID NO: 2.

5. The relative skill in the art.

The relative skill in the art as it relates to the method of the invention is characterized by that of a M.D. or Ph. D. level individual.

6-7. The amount of guidance present and the existence of working examples.

The applicant has not provided guidance for making and using an isolated recombinant polypeptide comprising an immunogenic fragment of at least 40 contiguous amino acids of SEQ ID NO: 2, wherein the immunogenic fragment, when administered either alone or coupled to a co-protein carrier is capable of inducing an antibody that specifically binds to said fragment within SEQ ID NO: 2

8. The quantity of experimentation necessary.

The amount of experimentation that is required is undue because making and using an isolated recombinant polypeptide comprising an immunogenic fragment of at least 40 contiguous amino acids of SEQ ID NO: 2, wherein the immunogenic fragment, when administered either alone or coupled to a co-protein carrier is capable of inducing an antibody that specifically binds to said fragment within SEQ ID NO: 2 is not routine and requires more experimentation. Therefore, in view of the overly broad scope of

the claims, the lack of guidance and working examples provided in the specification, and the high degree of unpredictability as evidenced by the prior art, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention. It must be noted that the issue in this case is the breath of the claims in light of the predictability of the art as determined by the number of working examples, the skill level of the artisan and the guidance presented in the instant specification and the prior art of record. The Applicants make and test position is inconsistent with the decisions of *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) where it is stated that "... scope of claims must bear a reasonable correlation to scope of enablement provided by the specification to persons of ordinary skill in the art...". Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See *In re Wands*, 858 F.2d at 737, 8 USPQZd at 1404 (Fed. Cir. 1988). Therefore, for the instant specification to be enabling, it needs to provide direction/guidance regarding an acceptable number of different fragments of SEQ.ID.NO: 2 that can induce an antibody that specifically binds to said fragment within SEQ ID NO: 2 . Absent sufficient guidance/direction one of skill in the art would not be able to practice the claimed invention commensurate in scope with the claims. Thus, for all these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention as the amount of experimentation required is undue, due to the broad scope of the claims, the lack of guidance and insufficient working examples provided in the specification and the high degree of unpredictability as evidenced by the state of the prior art, attempting to test all the different type of fragments of SEQ.ID.NO: 2 encompassed by the claimed invention would constitute undue experimentation. Therefore, applicants have not provided sufficient guidance to enable one of skill in the art to make and use the claimed invention in a manner that reasonably correlates with the scope of the claims, to be considered enabling.

Claim Rejections - 35 USC 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21 (2) of such treaty in the English language.

The transitional limitation "comprises" similar to the limitations, such as, "has", "includes," "contains," or "characterized by," represents open-ended claim language and therefore does not exclude additional, unrecited elements. See M.P.E.P 2111.03 [R-I]. See Molecular Research Corp. v. CBS, Inc., 793 F2d 1261, 229 USPQ 805 (Fed. Cir. 1986); In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981); Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948) ("comprising" leaves "the claim open. for the inclusion of unspecified ingredients even in major amounts". On the other hand, the limitation "consisting of represents

closed claim language and excludes any element, step, or ingredient not specified in the claim. In re Gray, 53 F. 2d 520, II USPQ 255 (CCPA 1931); Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948).

8. Claims 58, 61 ,75-76 and 79 - 81 are rejected under 35 U.S.C. 102(e) as being anticipated by Breton U.S.Patent 6673910.

Breton as shown below discloses an isolated polypeptide comprising an amino acid sequence SEQ.ID.NO: 2991 comprising an immunogenic fragment which has 40 contiguous amino acids and is 100% identical with the claimed polypeptide (please see the sequence alignment, QY indicates SEQ.ID.NO: 2 of the claimed invention and Db represents the prior art protein) and thus anticipated claims 58. The prior art discloses maltose receptor (outer membrane protein of *E.coli*) as a peptide fusion partner (column 34, lines 15-30 in patent) and thus discloses fusion protein as claimed in claim 61. Further the prior art discloses a vaccine composition (i.e., immunogenic composition) comprising *M.catarrhalis* polypeptide, SEQ.ID.NO: 2991 with pharmaceutical carrier such as buffer, adjuvant, glycerol etc (see column 37-38) . Further, the prior art discloses one or more surface proteins as vaccine a composition (see column 37, lines 8-20) for *M.catarrahalis* and thus anticipated immunogenic composition comprising immunogenic fragments /polypeptide and one other *M.catarrhalis* antigen in a pharmaceutical carrier as claimed in claims 75-76 and 79 - 81. Therefore, the claimed invention is anticipated by the prior art.

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US-09-540-236-2991
; Sequence 2991, Application US/09540236
; Patent No. 6673910
; GENERAL INFORMATION:
;  APPLICANT: Gary L. Breton et al.
;  CURRENT APPLICATION NUMBER: US/09/540,236
;  CURRENT FILING DATE: 2000-04-04
;  NUMBER OF SEQ ID NOS: 3840
; SEQ ID NO 2991
;   LENGTH: 118
;   TYPE: PRT
;   ORGANISM: M.catarrhalis
US-09-540-236-2991

  Query Match             20.7%;  Score 57;  DB 4;  Length 118;
  Best Local Similarity   100.0%;  Pred. No. 2.2e-47;
  Matches   57;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          47 PEQAVAEVAGQVAKEKYNLTVELVEFNDYAMPNSAVSKGELDANAMQHKPYLEKDSQ 103
               |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          57 PEQAVAEVAGQVAKEKYNLTVELVEFNDYAMPNSAVSKGELDANAMQHKPYLEKDSQ 113
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Conclusion

8. Claims 55, 57, 59, 62, 63, 68 , 73, 74, 77, and 78 are allowed.

Claims 58, 61, 75-76, 79-84 are rejected.

9. Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform to the notice published in the Official Gazette, 1096 OG 30, November 156, 1989. The Right Fax number is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PMR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PMR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Padma Baskar Ph.D., whose telephone number is ((571) 272-0853. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 6.30 a.m. to 4.00 p.m. except First Friday of each bi-week.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571) 272-0956.

Respectfully,

/Padma V Baskar/

Examiner, Art Unit 1645

/Robert B Mondesi/

Supervisory Patent Examiner, Art Unit 1645